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| 34363/BBRD-0 |              |
| EXAMINER     |              |
| HENDRICKS, K |              |
| ART UNIT     | PAPER NUMBER |

1814  
DATE MAILED:

02/14/95

**This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS**

☒ This application has been examined ☒ Responsive to communication filed on 11-22-94 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s),        days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
4. ☐ Notice of Informal Patent Application, PTO-152.
6. ☐

## Part II SUMMARY OF ACTION

1. ☒ Claims 4-7, 9-16, 19 & 23-29 are pending in the application.  
Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
2. ☐ Claims \_\_\_\_\_ have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 4-7, 9-16, 19 & 23-29 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other \_\_\_\_\_

### EXAMINER'S ACTION

Claims 4-7, 9-16, 19, and 23-29 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to methods of producing an alkalophilic asporogenic Bacillus novo species PB92 of minimal natural  
5 extracellular protease level, transformed with a B. novo PB92 alkaline protease which has been mutated as described in the specification. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicants' arguments concerning the mutation of the high alkaline protease gene have been deemed persuasive. Applicants  
10 have convincingly demonstrated that the mutation to the protease per se is not the significant part of the application and invention, as stated, for example, at the sentence bridging pages 12-13.

The claims are not properly enabled for the recitation of  
15 any "mutant high alkaline protease", and any "alkalophilic Bacillus strain". Applicants have stated that the strain PB92 has been used merely as an example, and that the specification provides enablement for the use of other types of these strains, and for other "mutant high alkaline proteases". Applicants  
20 further state that techniques for such are "routine and require no inventive skill or undue experimentation" (pg. 7, response of 9-7-93). This is not deemed persuasive for the reasons of record. Primarily, the specification has not provided pertinent information regarding any other "high alkaline protease" gene,  
25 nor any appropriate Bacillus strain that would satisfy the

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requirements of the invention. This fact is important, as the claims are not commensurate in scope with the specification and its enablement. This information is essential to the function of the claimed invention, and the essential material may not be improperly incorporated into the specification, and does not find support within the teachings of the specification. There is no teaching or reasonable expectation provided that one skilled in the art would be able to utilize the teachings provided for any other systems/genes, or even that there is a problem with any other source such that the instant invention would be applicable. Absent this knowledge, one skilled in the art is left with an undue amount of experimentation, due to the breadth of the claims, in order to attempt to determine what other Bacilli or proteases would be useful in the instant invention, and then further attempt to find the gene and apply the principles taught herein. Thus, one skilled in the art would in no way be enabled to practice the claimed invention with any such gene or strain other than the enabled Bacillus PB92.

The specification is not properly enabled for claims to any "derivative thereof" of a Bacillus novo species PB92. Applicants state that passages on page 12 of the specification refer to known "derivatives", and that this would be enabling for the instant invention. The phrase "derivatives thereof", however, encompasses predetermined and random mutants of the strain, and progeny of the strain that may or may not contain the gene for

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the "mutant high alkaline protease" and/or a revertant strain with the indigenous gene. The specification does not properly teach nor describe to one skilled in the art these "derivatives", what specifically they entail, nor how to obtain and/or use such.

5 Mere reference to other teachings, when this is a matter of essential material, without an instant and specific teaching as to how these would be applicable, is not sufficient. Thus, this results in undue experimentation for one skilled in the art to attempt to produce such without proper guidance from the  
10 specification.

The method of claims 12 and 27 are not properly enabled by the specification. This stands for the reasons of record, as applicant has not properly and specifically traversed the rejection. The claimed invention is not reflective of the method  
15 and "conditions whereby the replication function encoded by said vector is inactivated". It would require an inordinate amount of experimentation for one of ordinary skill to attempt to determine what and where the "replication function" of the vector is, its relationship to the rest of the invention, a method of  
20 "inactivating" such, and its possible effects upon the instant invention. Further, the specification is not enabling for any or all possible methods of "identifying" transformants with no detectable indigenous protease. The claims are not commensurate in scope with the enablement of the specification for such  
25 methods.

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New claim 29 is not properly enabled by the teachings of the specification for the host strain to be "substantially incapable of reversion". The specification, at page 7, lines 16-17, teach that the invention is (preferably) a "non-reverting mutation".

5 This clearly conflicts with the phrase "substantially incapable". Thus, one skilled in the art has not been taught by the specification, nor is enabled for, the production of such strains that are only "substantially incapable" of reversion. Similarly, since this is the case, and the gene encoding the high alkaline  
10 protease has been deleted, then it follows that there should be no "indigenous" alkaline protease product. Thus, it also follows that such a strain could not be "substantially free" of an indigenous alkaline protease, but instead, only completely free. The teachings of the specification do not provide support for  
15 such a strain being "substantially free", nor does the specification teach one skilled in the art how to produce such a strain.

It should be noted that applicants have pointed out, at page 17 of the response filed 11-22-94, that the Examiner has erred in  
20 rejecting claim number 9 under 35 USC 112, 1st paragraph. This is not deemed persuasive. Although the claim is specific with regard to the source of the protease gene, it has not overcome all the deficiencies specified above for the claim(s) from which it is dependent (ultimately claim 23). This can be easily seen,  
25 for example, if the limitations of claim 9 were to be included

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with the limitations of the claims it depends upon in one singular claim. Thus, it is specific (clearly enabled) for one aspect, but not all, and is still properly rejected.

5           Claims 16, 19 and 23-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10           Claim 16 recites deletion of the gene of claim 15 (ultimately dependent upon claim 12) "by homologous or illegitimate recombination". The independent claim 12 only recites the method by "homologous recombination", and thus claim 16 is indefinite in its improper limitation. Applicants have incorrectly stated that since the claim is now ultimately  
15           dependent from claim 27, the issue is resolved. This is not the case, as the claim is still dependent from either claim 12, 13 or 27.

20           Claims 19 and 24-25 are indefinite in the recitation of the phrase "one or more" of the protease produced. Since only one (type of) protease is being produced in the independent claims, the claims are indefinite for the recitation of "one or more". This is maintained for the reasons of record.

25           The method of claims 23 and 26 are indefinite, as it is a method for producing a protease by culturing the host strain, yet there is no "recovery step" involved for obtaining the protease

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from the host. Applicants state that a recovery step is not essential. This is not deemed persuasive, as again, this is a necessary step to the claimed invention, as the mere production of the protease in the strain can not result in the claimed protease being accessible, and thus possessing utility.

The amendment filed 9-7-93 is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

[a protease] "exhibiting altered protease activity".

This phraseology is not supported at page 29 or anywhere else in the specification. Page 29, at best, describes "altered" protease levels of production, but does not describe the proteases having different activity. Applicants response filed 11-22-94 has been considered but not deemed persuasive. It stated that since the specification, at page 29, reads "the specific activities of the protease mutants... were used to determine the production of protease...", then this must imply that the activity of the enzyme has changed (i.e. "exhibiting altered protease activity"). This is incorrect. A change in protease level (i.e. production) may indeed be measured by the amount of activity present (i.e. the amount of enzyme present reflected by its activity), but this in no way implies that the

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actual activity of the enzyme has been changed. The amount of total cellular protease activity level has changed, but not the activity of the enzyme itself. In other words, the enzyme still functions the same way, even though there is less of the enzyme.

5 Applicant is still required to cancel the new matter in the response to this Office action.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

10 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by  
15 the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed. This is deemed necessary for the reasons recited immediately above.

20 Claims 9, 19 and 23-26 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth immediately above in the objection to the specification regarding the new matter (applicant has only cancelled such in claim 14).

25 The amendment filed 11-22-94 is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:



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The phrases "minimal indigenous extracellular protease level", and "a specifically-mutated Bacillus novo PB92 alkaline protease" (underlining added for emphasis) in claim 28. *pg. 10 line 1-5  
Spec. refers to  
Mutated mutants only.*

Applicants, at page 8 of the response, have stated that  
5 since the Examiner "indicated as enabled" these phrases, that a claim quoting these phrases seemed proper. This is not. These phrases are merely quotes from the Office Action, in the Examiner's shorthand manner of expressing the enablement of the specification. Obviously, the specification deals with very low  
10 levels of expression product, but does not exactly mention "minimal indigenous" protease. Although the two might be grammatically interchangeable, this was not a suggestion or invitation to use this in the claims. This also applies to the phrase "specifically-mutated", which was a shorthand way of  
15 avoiding the listing of each mutation used or available to applicant.

Applicant is required to cancel the new matter in the response to this Office action.

The specification is objected to under 35 U.S.C. § 112,  
20 first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed. This is deemed necessary for the reasons recited immediately above.

Claim 28 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth immediately above in the objection to  
25 the specification.

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The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

5 A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the  
10 time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15 Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same  
20 person.

Claims 4-7, 9-16, 19, and 23-29 are rejected under 35 U.S.C. § 103 as being unpatentable over Fahnestock et al. and Estell et al., in view of TeNijenhuis and Suggs et al. The references and rejection are herein incorporated as cited in a previous Office  
25 Action.

Applicants' arguments filed in response to this rejection have been fully considered but they are not deemed to be persuasive. Arguments submitted 11-22-94 do not substantially differ from those already presented previously, and thus are not  
30 deemed persuasive for the reasons of record.

NO CLAIM IS ALLOWED.

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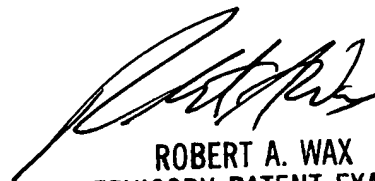
Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

5 A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL  
ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS  
ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS  
10 OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION  
IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED  
STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE  
ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE  
PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE  
MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE  
15 STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM  
THE DATE OF THIS FINAL ACTION.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Keith Hendricks whose telephone number is (703) 308-2959.

20 Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

25

  
ROBERT A. WAX  
SUPERVISORY PATENT EXAMINER  
GROUP 180

30

  
KDH  
February 8, 1995